V/5

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/822,033	03/24/1997	WAYNE A. MARASCO	43471-FWC	5884

7590 06/20/2005

Ronald I. Eisenstein
NIXON PEABODY LLP
101 Federal Street
Boston, MA 02110

EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 08/822,033	**Applicant(s)** MARASCO ET AL.	
	Examiner Joseph T. Woitach	**Art Unit** 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 09 June 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☒ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☒ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1 and 3-16*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Joe Woitach
AU1632

S.00

Continuation of 3. NOTE:
Support in the specification for the proposed amendment to claim 1 appears to raise issues of new matter. Figure 2 appears to provide at least two seqeuneces encoding the heavy and light chain of an antibody, and thus appears that what is specifically contemplated is a resulting protein with two amino and two carboxy terminals. This is consistent with providing other forms of antibodies such as a single chain antibody recited in other dependent claims. A new search and considereation for a single linear protein sequence would have done for related art and purposes of enablement regarding the ability of such a protein to specfically bind a target cell.

Continuation of 11. does NOT place the application in condition for allowance because: Applicants argue that providing a recombinantly made fusion protein provides unexpected properties over one made chemically. Further, it is argued that post-filing art and the declaration of Dr. Marsco provide evidence supporting this assertion. Additionally, it is argued that while the cited reference teaches making a fusion protein, this fusion protein was not used to deliver a nucleic acid. Applicants' arguments have been fully considered, but not found persuasive. As noted previously, Applicants arguments do not contest whether the cited references provide limitations that anticipate the embodiments of the claims nor the specific motivation for providing a recombinant fusion protein over a fusion protein made by chemical linkage. Applicants arguments focus primarily on the assertion that a recombinantly made protein would be more effective than one made chemically. Initially, it is noted that the present specfication does not provide any support for the fact that a recombinantly made protein would have any unique or unexpected property than one made recombinantly only that it could be assembele more readily or adapted more easily (see apge 5 for example). With regard to evidence in Li et al and discusion in the declaration of Dr. Marsco regarding the evidnece, Examiner would maintain that while one can compare qualitatively a quantitative comparison of the two compositions can not be done. As discussed previously, the differences between on how (or even why they were done) the experiments were conducted would not allow for a quantitative comparison. To make a informative quantitative comparision, the two compositions must be first somehow normalized to either binding capacity or even total protein used, then administered and compared directly. The difference in amount of fluorescence can not be attributed uniquely to the fusion protein and one has to take into the total of the two different experiments, for example amount/differences in the nucleic acid, the total amount of fusion protein used, the time at which expression was measured as examplifed by fluorescence which in this case is affected by how long the luciferase assay was allowed to proceed when the measurement was finally made. At the time of filing, there is no dispute that fusion protien can be made (noting that Wu prefers the use of a peptide bond as a linker p. 8), that fusion proteins were used to deliver polynucleotides, it is only contested that a recombinantly made fusion protein would be superior to one that was produced chemically. Given the evidence of record and in view of the breadth of the claims for a recombinant fusion protein made by any means (i.e. in cells that would not make an active or secreted form that would require re-folding for example), Applicants arguments are not found persuasive for the reasons above and of record .